Adult Xp11 Translocation Renal Cell Carcinoma Diagnosed by Cytogenetics and Immunohistochemistry

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Abstract

Purpose: To determine the incidence of Xp11 translocation renal cell carcinoma (RCC) in adult patients using cytogenetics and immunohistochemistry.

Experimental Design: Cytogenetic studies were prospectively done using tumor samples from 443 consecutive adult Japanese patients (ages 15–89 years) who underwent nephrectomy for RCC. TFE3 immunohistochemistry was done for cases in which cytogenetic results were not obtained. Clinico-pathologic characteristics of Xp11 translocation RCC were examined.

Results: Mitotic cells suitable for cytogenetic analysis were obtained in 244 tumor samples (55%); among these, we identified 4 cases (1.6%) of Xp11 translocation RCC. TFE3 immunohistochemistry identified 3 positive cases (1.5%) among the remaining 199 cases. The median age of the 7 patients was 41 years (range, 15–59 years), and 15% of RCC patients (4 of 26) who were younger than ages 45 years had this type of RCC. Of the four Xp11 translocation RCC patients whose karyotypes were determined, two had an ASPL-TFE3 gene fusion. Of these 2, 1 had pulmonary metastasis at presentation, and the other developed liver metastasis 12 months after nephrectomy and died of the disease. The remaining two patients had PRCC-TFE3 and PSF-TFE3 gene fusions, respectively. Both had nodal involvement but remained disease free for 3 and 5 years, respectively, after surgical resection of lymph node metastases. Of the 3 immunohistochemically diagnosed patients, 1 had nodal metastases at presentation and died 9 months after surgery.

Conclusions: This is the first report to determine the incidence of Xp11 translocation RCC in adult patients. We found that this disease is relatively common in young adults.

The gene fusion resulting from the specific chromosome translocation of alveolar soft part sarcoma was identified in 2001 (1). The translocation of t(X;17)(p11;q25) results in a fusion between TFE3, which is a member of the microphthalmia-TFE basic helix-loop-helix leucine zipper transcription factor subfamily on chromosome Xp11, and the novel ASPL gene on 17q25. Although the function of ASPL remains unclear, the TFE3 gene is also implicated in translocations involving Xp11 in a subset of renal cell carcinomas (RCC), especially in children and young adults (2). Thereafter, various other translocations involving chromosome Xp11 were identified; all of them result in gene fusions involving the TFE3 gene, such as PRCC-TFE3, PSF-TFE3, CLTC-TFE3, and NonO-TFE3 (3). Xp11 translocation RCC was included in the WHO classification of RCC for the first time in 2004 (4). Although several Xp11 translocation RCCs have recently been identified and characterized at the morphologic and molecular level (5–8), the correlation between fusion type and biological behavior is, to date, still unclear.

This neoplasm predominantly affects young patients. Argani et al. (3) reported that approximately one-third (21 of 66) of renal carcinomas in children seemed to belong to the Xp11 translocation carcinoma family; this figure was based on morphologic findings and TFE3 immunohistochemistry. In children younger than 15 years, RCC is relatively uncommon and comprises only 2.6% of renal neoplasms (9). The tendencies of RCC in childhood include an equal sex ratio, increased survival with isolated lymph node involvement, reduced frequency of symptoms of para-neoplastic phenomena, and predominance of papillary architecture (10–12).

Additionally, some adult cases of Xp11 translocation RCC have been reported. Argani et al. (13, 14) recently identified 28 adult cases using TFE3 immunohistochemical staining. Although these authors suggested that a considerable number of cases might go undetected in adults, the true incidence of this neoplasm remained unclear. Accordingly, we undertook the present study to determine the incidence of this type of tumor in adult RCC patients using cytogenetics and immunohistochemical staining.
Translational Relevance

We determined the incidence of Xp11 translocation renal cell carcinoma (RCC) in adult patients using cytogenetics and immunostaining for TFE3. Cytogenetic analyses were prospectively done on tumor samples from 443 consecutive adult patients who underwent nephrectomy for RCC; mitotic cells suitable for cytogenetic analysis were obtained in 244 of the 443 tumor samples (55%). The remaining 199 cases were screened for Xp11 translocation RCC by immunostaining for TFE3. Cytogenetics and immunohistochemical analysis identified 4 (1.6%) and 3 (1.5%) cases of Xp11 translocation RCC, respectively. The median age of the 7 patients was 41 years (range, 15–59 years); 15% of RCC patients (4 of 26) who were younger than age 45 years had this type of RCC. These results show that this disease is not uncommon in young adults. Of the four cytogenetically analyzed cases, two patients had an ASPL-TFE3 gene fusion and had visceral metastases. The remaining two patients had PRCC-TFE3 and PSF-TFE3, respectively. Both of these latter cases had nodal involvement but maintained disease-free status for at least 3 years after surgical resection. Young patients with renal tumors and lymph node metastasis alone should be treated with thorough lymph node dissection as well as radical nephrectomy, considering the likelihood that they have this type of RCC. Our results also indicate that a particular gene fusion such as ASPL-TFE3 might be associated with an unfavorable prognosis.

Patients and Methods

Patients. Between 1995 and 2006, 445 consecutive Japanese patients underwent radical or partial nephrectomy for sporadic RCC at our institution. Two patients were excluded from this study because they had known genetic predispositions to RCC, such as von Hippel-Lindau disease or Birt-Hogg-Dube syndrome. The characteristics of the remaining 443 patients are summarized in Table 1. The mean and median ages of the patients were 60 and 61 years, respectively. Males were affected about thrice more frequently than females. Thirty-nine of the patients (8.8%) had reached stage IV of the disease.

Cytogenetics. Karyotype analyses with Q-linking were used in all 443 cases. Written informed consent for cytogenetic studies was obtained from all patients. The consent form was approved by the institutional review board. All cytogenetic studies were done in the same way except for karyotype analysis. Sections 4 m in thickness were mounted onto positively charged slides, and immunohistochemical staining was done according to the avidin-biotin complex method. Heat-mediated antigen retrieval was done in Tris-EDTA buffer (pH 9) in a water bath at 97°C for 40 minutes. Tissue microarray was constructed with 2 cylindrical core biopsies, each 0.2 cm in diameter, taken from 1 representative paraffin-embedded tissue block of each tumor. Sections were incubated overnight with a 1:600 dilution of the P-16 polyclonal antibody to TFE3. Tumors were considered positive for TFE3 if they showed nuclear immunoreactivity that was readily apparent at low-power magnification (×40). Cytoplasmic immunoreactivity was ignored because both native TFE3 and its fusion protein are known to localize to the nucleus. Some randomly selected tumor samples of cyogenetically non-Xp11 translocation RCC were used as a negative control, and specimens of alveolocytic soft part sarcoma arising three different patients were used as a positive control.

Reverse transcription-PCR and sequence analysis. The results of the cytogenetic study were confirmed by reverse transcription-PCR (RT-PCR), which we did as previously described (15) in two of the four cases in which we identified Xp11 translocation RCC through the karyotype (Table 2). Briefly, 1 μg of total RNA extracted from the tumor tissue was reverse transcribed and subjected to PCR using the PRCC- or ASPL- and TFE3-specific primers listed below. In case 3, to detect the presence of a PRCC-TFE3 gene fusion transcript, we used PRCC-628F: 5′-AGAAGAGGAAAGGACCT-3′ and TFE3-1146R: 5′-AGCA- GATTCCCTGACACAG-3′ primers. The PCR product was cloned into the pGem-T vector (Promega), and sequence analysis was done using a CEQ8000 DNA sequencer (Beckman Coulter). In case 4, to detect the presence of an ASPL-TFE3 gene fusion transcript, RT-PCR was done in the same way except we used ASPL-L51: 5′-AAAGGAGTC- GATCGGGCCAG-3′ primer instead of the PRCC-622F primer.

Statistical analysis. Intergroup differences in categorical, ordinal, and continuous variables were analyzed using Fischer’s test, the Mann-Whitney test, and the t test, respectively. All statistical analyses were done using JMP 6 software (SAS Institute, Inc.). For all analyses, P values of <0.05 were considered to indicate significance.

Results

Patients identification. Mitotic cells suitable for the analysis were obtained from 244 of the 443 RCC samples (55%). Among these, we identified 4 cases (1.6%) of Xp11 translocation RCC by searching a cytogenetic study database. Out of the remaining 199 cases in which the karyotype was not obtained, immunohistochemical study using a TFE3 antibody identified 3 cases (1.5%) of Xp11 translocation RCC. The characteristics of the 244 cytogenetically analyzed patients were similar to those of the 199 immunohistochemically analyzed patients (Table 1).

Chromosome findings. Of the 244 tumors for which the karyotype was successfully obtained, 96 tumors (39%) had one of the chromosome aberrations that are typical of RCC. The karyotypes of RCC were categorized as follows: conventional clear cell type RCC exhibited chromosome 3p deletion; papillary type RCC exhibited loss of chromosome Y and gain of chromosomes 7 and 17; chromophobe type RCC exhibited both loss of chromosome 1, 6, 10, 13, or 17 and loss of 1, 2, 6, 10, 13, or 17.
and Xp11 translocation type RCC exhibited translocations involving chromosome Xp11. Of the 96 chromosomally aberrant tumors, 74 had aberrations typical of conventional clear cell type RCC, 10 had aberrations typical of papillary type RCC, 8 had aberrations typical of chromophobe type RCC, and 4 had aberrations typical of Xp11 translocation type RCC. The chromosomal aberrations of the four cases of Xp11 translocation RCC diagnosed using karyotype are shown in Table 2. The fusion types of cases 1 and 2 were determined to be PSF-TFE3 and PRCC-TFE3.

Table 1. Patient and tumor characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total (N = 443)</th>
<th>Cytogenetically analyzed (n = 244)</th>
<th>Immunohistochemically analyzed (n = 199)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (range) age, y</td>
<td>59.5 ± 11.6 (15-89)</td>
<td>60.2 ± 12.1 (15-89)</td>
<td>59.1 ± 11.1 (30-82)</td>
<td>0.32*</td>
</tr>
<tr>
<td>No. patients</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Male</td>
<td>321</td>
<td>181</td>
<td>140</td>
<td>0.41†</td>
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<tr>
<td>Female</td>
<td>122</td>
<td>63</td>
<td>59</td>
<td></td>
</tr>
<tr>
<td>Stage [Union Internationale Contra Cancrum (Italian)]</td>
<td></td>
<td></td>
<td></td>
<td>0.99†</td>
</tr>
<tr>
<td>I</td>
<td>330 (74%)</td>
<td>180 (74%)</td>
<td>150 (75%)</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>32 (7.2%)</td>
<td>18 (7.3%)</td>
<td>14 (7.0%)</td>
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<tr>
<td>III</td>
<td>42 (9.4%)</td>
<td>24 (9.8%)</td>
<td>18 (9.0%)</td>
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<tr>
<td>IV</td>
<td>39 (8.8%)</td>
<td>22 (9.0%)</td>
<td>17 (8.5%)</td>
<td></td>
</tr>
<tr>
<td>Subtype of RCC</td>
<td></td>
<td></td>
<td></td>
<td>0.92†</td>
</tr>
<tr>
<td>Conventional</td>
<td>380 (85%)</td>
<td>213 (87%)</td>
<td>167 (84%)</td>
<td></td>
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<tr>
<td>Papillary</td>
<td>22 (4.9%)</td>
<td>12 (4.9%)</td>
<td>10 (5.0%)</td>
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</tr>
<tr>
<td>Chromophobe</td>
<td>25 (5.6%)</td>
<td>12 (4.9%)</td>
<td>13 (6.5%)</td>
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</tr>
<tr>
<td>Collecting duct</td>
<td>2 (0.4%)</td>
<td>2 (0.8%)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Xp11 translocation</td>
<td>7 (1.5%)</td>
<td>4 (1.6%)</td>
<td>3 (1.5%)</td>
<td></td>
</tr>
<tr>
<td>Unclassified</td>
<td>7 (1.5%)</td>
<td>1 (0.4%)</td>
<td>6 (3.0%)</td>
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<tr>
<td>*t test</td>
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<tr>
<td>†Fisher's test</td>
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<td></td>
</tr>
<tr>
<td>‡Mann-Whitney test</td>
<td></td>
<td></td>
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</table>

Table 2. Clinicopathologic features of 7 cases of Xp11 translocation RCC

<table>
<thead>
<tr>
<th>Year of nephrectomy</th>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
<th>Case 4</th>
<th>Case 5</th>
<th>Case 6</th>
<th>Case 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laterality</td>
<td>15/F</td>
<td>40/M</td>
<td>41/F</td>
<td>24/F</td>
<td>57/M</td>
<td>59/M</td>
<td></td>
</tr>
<tr>
<td>Symptom</td>
<td>Palpable mass</td>
<td>Incidental</td>
<td>Incidental</td>
<td>Incidental</td>
<td>Incidental</td>
<td>Incidental</td>
<td>Left</td>
</tr>
<tr>
<td>Primary tumor size (cm)</td>
<td>15</td>
<td>10</td>
<td>6</td>
<td>6</td>
<td>2</td>
<td>3</td>
<td>16</td>
</tr>
<tr>
<td>TNM at presentation</td>
<td>T2N2M0</td>
<td>pT2 pN2 cM0</td>
<td>T2N0M0</td>
<td>T2bN0M0</td>
<td>T1bNOM1 (PUL)</td>
<td>T1aNOM0</td>
<td>T1aNOM0</td>
</tr>
<tr>
<td>Maximal TNM stage</td>
<td>62</td>
<td>92</td>
<td>26</td>
<td>14</td>
<td>16</td>
<td>14</td>
<td>16</td>
</tr>
<tr>
<td>Follow-up after nephrectomy (mo)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outcome</td>
<td>NED (lost follow-up)*</td>
<td>NED†</td>
<td>DOD‡</td>
<td>AWD‡</td>
<td>NED</td>
<td>NED</td>
<td>DOD</td>
</tr>
<tr>
<td>Initial pathologic diagnosis (H&amp;E)</td>
<td>cRCC</td>
<td>cRCC</td>
<td>pRCC</td>
<td>pRCC</td>
<td>cRCC</td>
<td>cRCC</td>
<td>cRCC</td>
</tr>
<tr>
<td>IHC for TFE3</td>
<td>Positive</td>
<td>Positive</td>
<td>Positive</td>
<td>Positive</td>
<td>Positive</td>
<td>Positive</td>
<td>Positive</td>
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<tr>
<td>Chromosome number</td>
<td>46</td>
<td>44-46</td>
<td>70-82</td>
<td>78-81</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
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<tr>
<td>Xp11 translocation</td>
<td>t(X;1)</td>
<td>t(X;1)</td>
<td>t(X;17)</td>
<td>t(X;17)</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Assumed fusion type/confirmed RT-PCR</td>
<td>*PSF-TFE3/NA</td>
<td>*PRCC-TFE3/yes</td>
<td>ASPL-TFE3/NA</td>
<td>ASPL-TFE3/yes</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

Abbreviations: TNM, tumor-node-metastasis; cRCC, RCC clear cell type; pRCC, RCC papillary type; NA not analyzed; NED, no evidence of disease; DOD, died of disease; IHC, immunohistochemistry.

*In case 1, the patient was lost to follow-up 5 y after the surgery without evidence of disease at the last presentation.
†In case 2, the initial TNM stage was T2N0M0 and regional lymph node metastasis occurred 5 y after nephrectomy. The patient was disease-free for 25 mo after resection of the lymph node.
‡In case 4, the disease was progressively developing.
respectively. An assumed ASPL-TFE3 gene fusion was detected in cases 3 and 4. The Q-band finding of case 4 is shown in Fig. 1A. Chromosomal numbers were 46, 44 to 46, 70 to 82, and 78 to 81 in cases 1, 2, 3, and 4, respectively.

RT-PCR findings. RT-PCR analysis of the tumor RNA samples was carried out in cases 2 and 4 to confirm that their chimeric transcripts contained both PRCC and TFE3, and both ASPL and TFE3, respectively. As shown in Fig. 1B, the ASPL-TFE3 fusion was detected in the case 4 sample, and the in-frame fusion between ASPL and TFE3 was confirmed by direct sequencing of the PCR product (Fig. 1C). Likewise, in case 2, the PRCC-TFE3 fusion was detected by RT-PCR and confirmed by direct sequencing (data not shown).

Clinical characteristics of Xp11 translocation RCC. The clinical features of the seven patients diagnosed with Xp11 translocation RCC are shown in Table 2. The median age of the 7 patients was 41 years (range, 15-59 years). Of the 443 patients treated for RCC, 26 were younger than age 45 years, and of these 26, 4 (15%) had Xp11 translocation RCC. In comparison, only 3 (0.7%) of the 417 who were ages 45 years or over had Xp11 translocation RCC (P = 0.0026). The male-female ratio among the 7 patients was 4:3. Computed tomography revealed that all of the tumors were well-defined heterogeneous lesions (Fig. 2A). At presentation, two patients (cases 1 and 7) had nodal involvement, and one (case 4) had lung metastasis. Of the remaining four patients, two developed lymph node (case 2) or liver (case 3) metastasis in their clinical courses. Two of the seven patients (cases 3 and 7) died of the disease and one (case 4) showed progression of the disease despite administration of IFN-α and interleukin-2. Of the three patients with unfavorable clinical course, two (cases 3 and 4) showed ASPL-TFE3 gene fusions. Two of the 3 patients with lymph node metastases maintained disease-free status for at least 3 years after lymph node dissection (case 1, 62 months; case 2, 36 months); both of these patients had TFE3 fusion types other than ASPL-TFE3.

Pathologic findings. In terms of appearance, the tumors were solitary and ranged from 2 to 16 cm in length (mean, 8.2 cm). None of the tumors showed evidence of extracapsular invasion (≥ pT2); rather, all presented as well-circumscribed lesions. The cut surfaces of the tumors were whitish gray to gray-tan with areas of hemorrhage. Necrosis was seen in cases 1, 2, 4, and 7 (Fig. 2B). The tumor involved the mucosa of the renal pelvis in cases 3 and 7.

Under microscopic examination, all tumors showed a tubulopapillary pattern (Fig. 3A-C). Tumor cells had clear voluminous cytoplasm with discrete cell borders; the cells in cases 1, 2, 4, 6, and 7 had small pyknotic nuclei (Fig. 3A and B). Part of each tumor consisted of granular cells (Fig. 3A and C). Cases 2, 4, and 7 exhibited extensive stromal hyaline nodules and many psammoma bodies (Fig. 3B). Five cases (cases 1, 2, 5, 6, and 7) were initially diagnosed as clear cell RCC, whereas the remaining two cases (cases 3 and 4) were initially diagnosed as papillary RCC.

Immunohistochemical staining showed that tumor cells from all cases expressed strong nuclear TFE3 staining (Fig. 3D), whereas the surrounding mesenchymal cells were negative for TFE3. Tumor cells of cytogenetically examined non-Xp11 translocation RCC did not show nuclear TFE3 staining.

Discussion

This is the first report of the incidence of Xp11 translocation RCC in adult RCC patients. We used cytogenetic analysis to search for cases among 244 adult RCC samples, and identified 4 cases (1.6%). These results were confirmed by TFE3 immunostaining and/or RT-PCR. We screened the remaining 199 samples, for which the karyotype was not determined, by immunostaining for TFE3, and identified 3 cases (1.5%) this way. The median age of the 7 patients with Xp11 translocation
RCC was 41 years. Four of them were younger than age 45 years. Thus, of the 26 RCC patients who were under age 45 years, 15% had this type of RCC. These results show that this tumor is relatively common in young adult patients.

Only a small number of adult Xp11 translocation RCC cases have been previously reported. This is probably due to the ease with which this tumor is misdiagnosed as either clear cell RCC or papillary RCC because of its histologic similarity to these other RCC subtypes and because it was only recently established as an independent RCC subtype. In fact, each of our seven patients had received an initial pathologic diagnosis of either clear cell or papillary RCC, based on H&E staining. The combined features of “clear cell” and “papillary” architecture are the most distinctive appearance from other subtypes of RCC (3).

To date, it has not been established whether different fusion types of Xp11 translocation RCC display different biological behaviors. Our data suggest that a particular fusion type, ASPL-TFE3, might be associated with an unfavorable prognosis. The two patients with ASPL-TFE3 gene fusion both developed visceral metastases, and one of them died of the disease. Similarly, a previous study reported that the patients with this fusion type usually presented with an advanced stage of the disease (4). In contrast, the two patients with PSF- or PRCC-TFE3 had nodal involvement, but both remained disease-free for at least 3 years after lymph node dissection. Generally, nodal metastases, even in the absence of distant metastases, portend ominous prognosis in RCC patients (16). The characteristics of our two cases with nodal involvement (cases 1 and 2) were similar to those of certain pediatric RCC cases with isolated lymph node involvement in which prolonged survival was reported (10). Very recently, Geller et al. (14) also reported that nodal disease without distant metastasis (TxN1-3M0) has a favorable short-term prognosis after surgery alone in Xp11 translocation RCC patients. Further studies are needed to evaluate the correlation between fusion type and biological behavior in Xp11 translocation RCC, but patients previously diagnosed with node-positive clear cell or papillary RCC and presenting with long-term disease-free survival should be investigated to determine whether their tumors were actually of the Xp11 translocation RCC subtype.

To differentiate this neoplasm from other RCC subtypes, Meyer et al. (17) suggested the consistent use of antibodies against TFE3 in all RCC cases because moderate to intense nuclear labeling for TFE3 protein is the most distinctive immunohistochemical feature of Xp11 translocation RCC (18). In this study, we confirmed the high sensitivity and specificity of the nuclear immunoreactivity for TFE3 protein of this subtype (18). We therefore agree that TFE3 immunohistochemical analysis is a useful technique for identifying this type of tumor.

The optimal treatment for Xp11 translocation RCC remains to be determined. According to several previous studies and our own results, preoperative differentiation between Xp11 translocation RCC and the other types of RCC is very difficult. Young patients with only renal tumors and lymph node metastasis should undergo thorough lymph node dissection as well as radical nephrectomy, considering the high probability that such cases are Xp11 translocation RCC. There have been no reports of immunotherapies such as IFN-α and interleukin-2 producing a significant response in this type of tumor. The present study conforms to this trend; patients 3, 4, and 7 received both IFN-α and interleukin-2 therapy, but none of them showed any response.

Despite this, recent gene expression profiling studies have suggested a novel therapeutic target in the treatment of Xp11 translocation RCC. We now know that the ASPL-TFE3 fusion protein transactivates the MET promoter, increasing MET mRNA expression. Other fusion types also bind to the MET promoter and strongly activate it (19). Because both MET and hypoxia-inducible factor-1α proteins are heat shock protein 90 clients, heat shock protein 90 inhibitors might be expected to have a positive influence on tumor progression because the MET (20) and hypoxia-inducible factor-1 (21) signaling pathways promote tumor progression and are commonly activated in aggressive tumors. In the MET signaling pathway, at least three routes of pathway intervention have been attempted as selective anticancer drug development strategies: antagonism of ligand binding, inhibition of tyrosine kinase catalytic function, and blockade of interactions between activated receptors and downstream intracellular effectors (22). In a T24 bladder carcinoma model, Koga et al. (23) reported the efficacy of the low-dose heat shock protein 90 inhibitor geldanamycin, which down-regulated MET by inhibiting new protein maturation, thereby dampening HGF signaling in vitro. Several human clinical trials are now under way (24, 25), and the experimental results of these trials might lead to the development of an effective treatment for Xp11 translocation RCC patients.

Two major strengths of our study were its inclusion of a relatively large sample size in the cytogenetic analysis and its presentation of clinical results with a long follow-up period. On the other hand, there are several possible limitations. There was
the possibility of a selection bias: this study included only Japanese patients treated at a single institution. Furthermore, only 55% of RCC samples were successfully analyzed for chromosomal study, although we did perform TFE3 immuno-histochemical analysis on the remaining tumor samples. However, no difference was seen between the characteristics of the 244 tumors in which chromosomal findings were obtained and those of the remaining 199 tumors. Interestingly, the incidence of Xp11 translocation RCC was almost equal in the 2 groups: 1.6% in cytogenetically analyzed cases and 1.5% in immunohistochemically analyzed cases.

In conclusion, our findings indicate that the existing cases of adult Japanese RCC include a considerable number of Xp11 translocation RCCs. Notably, this type of tumor is relatively common in young adult patients and should be included in differential diagnoses even in cases of adult RCC. Furthermore, ASPL-TFE3 gene fusion might be considered an unfavorable factor. More data are needed to determine the best treatment methods and outcomes of this tumor type. Specifically, international multicenter studies including larger numbers of cases are needed to confirm the current results and determine the optimal treatment strategy for Xp11 translocation RCC.

Disclosure of Potential Conflicts of Interest

Our study is not supported by any commercial relationship, financial grants, or funding.

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Fig. 3. A, the tumor showed tubulopapillary architecture, and was composed of clear and granular cells with abundant cytoplasm (case 2, ASPL-TFE3 fusion; B) Many psammomabodies were seen (case 3, PRCC-TFE3). C, granular cells were partly dominant in this tumor (case 3, PRCC-TFE3). D, TFE3 immunohistochemical analyses showed that tumor cells expressed strong nuclear staining.

References

Human Cancer Biology


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